

**Note on:**

**“LD<sub>50</sub>” [LETHAL DOSE 50%]**

This Note is designed to provide guidance to RSC members and may also be useful to others with a particular interest in the subject.

The LD<sub>50</sub> test and its variants are now considered obsolete. Internationally accepted alternative tests, using fewer animals and “absence of evident toxicity”, rather than death, as their criterion, have been developed. They are accepted by most regulators as valid alternatives to LD<sub>50</sub> testing which, previously, was usually undertaken as a result of then legislative requirements.

Nonetheless, LD<sub>50</sub> values are still quoted and enquiries received by the Royal Society of Chemistry suggest that there is still a need for information about their meaning. This note aims to provide basic information about LD<sub>50</sub>. Readers are urged to obtain more detailed information, if required.

#### WHAT IS AN LD<sub>50</sub>?

“LD<sub>50</sub>” is an abbreviation for “Lethal Dose 50%”, sometimes also referred to as the “Median Lethal Dose” (Figure 1). Although the LD<sub>50</sub> is no longer the preferred measure for assessing the acute toxicity of single doses of a substance, for historical reasons it is probably still the most commonly cited measure.

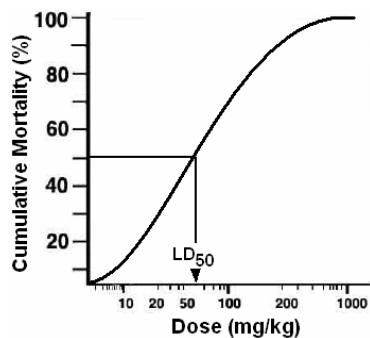


Figure 1. Median Lethal Dose or LD<sub>50</sub>

The LD<sub>50</sub> for a particular substance is essentially the amount that can be expected to cause death in half (i.e. 50%) of a group of a particular animal species, usually rats or mice, when entering the animal's body by a particular route. For example, if the substance is swallowed, the figure is an 'oral LD<sub>50</sub>' whereas if it's absorbed through the skin, it's a 'dermal LD<sub>50</sub>'. LD<sub>50</sub> figures are derived by mathematical calculation from the results of tests on animals and hence cannot be regarded as biologically precise values. In general, the amounts of a substance required to kill animals from different species are approximately related to the animals' body weights. Therefore, LD<sub>50</sub> figures are usually reported in units of milligrams of the substance per kilogram body weight for the animal species concerned.

Similarly, LC(t)<sub>50</sub> is essentially the concentration of a substance in air that can be expected to cause death in half (i.e. 50%) of a group of a particular species when entering the body by inhalation over the specified period of

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time. "LC(t)<sub>50</sub>" figures are usually reported as milligrams of the substance per cubic metre (or litre) of the air which the animal is breathing for the specified time (t). Generally, for inhalation, no account is taken of body weight when comparing values for different species.

Conventionally, the median lethal dose (MLD) is quoted as an LD<sub>50</sub> when the substance is absorbed by swallowing, skin contact or injection and as an LC(t)<sub>50</sub> when exposure is by inhalation. When quoting an LD<sub>50</sub> figure, details of the substance, the route of entry and the animal species must be given. For example, sodium cyanide has an oral LD<sub>50</sub> of 15 mg/kg in rats. The LC(t)<sub>50</sub> of a substance should state the duration (t) and species.

From the above it is clear that the lower the LD<sub>50</sub> or LC(t)<sub>50</sub> figure, the smaller is the amount of the substance needed to cause death.

In environmental toxicology, the concentration of a substance lethal to wildlife may also be expressed as a LC(t)<sub>50</sub> figure where the concentration (c) refers to the concentration in the relevant environmental medium. Perhaps the most commonly used is LC(t)<sub>50</sub> in water to indicate aquatic concentrations lethal to fish species. However, LC(t)<sub>50</sub> values can also be given for substances in soil or other materials.

#### WHAT USE IS AN LD<sub>50</sub> FIGURE?

Most users of a substance need to know its possible toxicity to humans. Expert judgement to assess the relevance to humans of toxicity data derived from animals, including LD<sub>50</sub> figures. Under EU law, the supplier of a chemical must assign it to a defined toxic hazard category using criteria set out in the legislation. The supplier may use LD<sub>50</sub> figures, among other data, when deciding how to do this. Alternatively, they can use a classification system based on a lack of "evident toxicity".

Either procedure may be used to classify the acute lethal hazard of a substance, as set out in the regulatory requirements (e.g. "very toxic if swallowed"). LD<sub>50</sub> and LC(t)<sub>50</sub> values give no information about other, non-lethal, effects of the substance, nor about cumulative, chronic, reproductive or irritant effects.

The law requires that the supplier of a substance must classify and label it to show the hazard categories to which it belongs and provide a material safety data sheet (MSDS) that gives, amongst other things, the substance's hazard categories. The relevant MSDS should provide much, but not all, of the information that must be taken into account when making a COSHH assessment and deciding on appropriate control measures in the workplace. [Information will also be needed on the circumstances of use, and hence, the likely exposures.] The MSDS also provides information needed when classifying wastes as "special wastes". Information on LC(t)<sub>50</sub> values can also be used when preparing safety reports for toxic major accident hazards.

#### FURTHER READING

'Principles and Methods of Toxicology', Hayes, A., Taylor and Francis, 4th Ed, Chapter 18 2001

'Acute Toxicology Testing', Gad, S., The Telford Press, Chapter 7, 1988

'A New Approach to Classification of Substances and Preparations on the Basis of their Acute Toxicology', The British Toxicology Society, Human Toxicol., Vol 3, 85-92, 1984

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